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10/062,954	01/31/2002	Gregory Blair Lamb	1855.4	4572

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/062,954	LAMB, GREGORY BLAIR	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11-13-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

1. Currently, claims 1-22, and 24-30 are pending in the application. Claims 1-8, and 10-20 have been withdrawn from consideration as directed to non-elected subject matter. Claims 9, 21, 22, and 24-28 were rejected in the prior action, mailed on July 31, 2003. In the Response filed on October 30, 2003, the Applicant cancelled claim 23 (also rejected in the prior action), and amended claims 9 and 24, and added new claims 29 and 30.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on November 13, 2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

3. It is noted that the Burg et al. reference in the Nov. 2003 IDS is in a foreign language with an English translation. The reference has therefore been considered to the extent of the English abstract.

Claim Objections

4. **(New Objection)** Claim 21 is objected to because of the following informalities: in the listing of potential disorders, a comma is required between the last and next to last members (before the "and" in line 3 of the claim). Appropriate correction is required.

5. **(New Objection)** Claim 29 is objected to because of the following informalities: there is no comma between the term "(FGF)" and the word "and" in line 5 of the claim. Appropriate correction is required.

6. **(New Objection)** Claim 30 is objected to because of the following informalities: there is no comma between the term "botulinum toxin" and the "and" in line 4 of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Withdrawn)** Claims 9, 21, 22, and 28 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In view of the amendment to the claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. **(Prior Rejection- Maintained)** Claims 9, and 21-27 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over the teachings of Donovan (U.S. Patent 6,500,436), Aoki et al. (U.S. Patent 6,290,961), further in view of Share (U.S. Patent 3,903,301) and of Borodic et al., (Drug Safety 11(3): 145-52). Claim 23 has been cancelled from the application. The rejection is therefor withdrawn from this claim as moot. The rejection is maintained over pending claims 9, 21, 22, and 24-27. The claims read on methods of treating a patient with a spinal compression disorder by administering botulinum toxin (BT) to the patient. The art references have been described in the prior action.

The Applicant traverses the rejection with reference to the claims generally on three grounds, and with respect to claim 25 on an additional ground. First, the Applicant argues that the claimed references, particularly the Donovan reference, fails to teach, and teaches away from, the administration of BT to treat muscles. Second, the Applicant argues that references fail to teach the administration to the intrinsic muscles of the spine. Finally, the Applicant argues that the art does not teach the additional benefit of the use of the toxin, the prevention of compression during the healing process. The additional argument with reference to claim 25 will be discussed below. These arguments have not been found persuasive for the reasons indicated below, and for the reasons of record.

General arguments in traversal

The Applicant first argues that the Donovan reference teaches the modification of the botulinum toxin and provides a definition for the term intraspinal, but does not teach the claimed

invention. While the Applicant's assertions may be true, the reference also teaches, as indicated in the prior action, that the toxin may be administered by other routes (including intramuscular), and that the toxin is useful for treating pain, including those associated with spinal cord injuries. Thus, the reference teaches the administration of the toxin to the same population as those in the claimed invention.

Also in reference to Donovan, the Applicant further argues that the reference teaches away from the claimed invention. The Examiner does not agree. While the reference does teach that alternative targeting moieties may be attached to the toxin, the reference does not require that this be done. Rather, the reference suggests such modifications to improve the toxin's pain relieving effects. These teachings are not inconsistent with the teachings of the other references (e.g. Aoki and Borodic), which indicate that the toxin may be administered to muscles without modification.

From the combined references, it would be obvious to those in the art to administer the toxin to any muscle that was the source of a spinal injury or disorder causing pain. This is demonstrated both by the teachings of Aoki ((teaching the relief of pain associated with muscle contractions) and of Borodic (indicating that the administration of the toxin to muscles results in an attenuation of the muscle strength). While the references do not specifically indicate that the intrinsic muscles should be targeted, it is clear that the toxin may be administered to any muscle that is causing such an injury.

The Applicant further argues that the references, in using the term paraspinal, do not include the intrinsic muscles. This argument is also not found persuasive. For example, in a discussion of an alternative usage of BT, U.S. Patent 5,053,005 (the Borodic patent, of record in

the November 13, 2003 IDS) indicates that the multifidus muscle is included in reference to the paraspinal muscles, and indicates that those in the art were in possession of the knowledge necessary for injection of the toxin to the muscles. Patent, column 3, lines 46-51. Because the art indicates that the toxin may be administered to any muscle causing pain, including through contraction and spasm, and further indicates that the toxin is effective in treating such pain associated with paraspinal muscles generally (both intrinsic and extrinsic), it would have been obvious to those in the art to administer the toxin to the intrinsic muscles when such were the source of such pain.

Thirdly, the Applicant argues that he references do not teach that the effects of the toxin would be long lasting (prevent recurrence of the compression until the damaged tissues heal). However, such would have been inherent in the administration of the toxin to the muscles. A fact that is recognized by the Donovan reference (col 7) where the reference indicates that the duration of the toxin's effects was known. See also, the Borodic patent, column 3, lines 51-56 (demonstrating that the duration of the toxin's effects is about 3 to 6 months). Thus, the Applicant is arguing that their invention is non-obvious because they have discovered a previously unrecognized benefit to the claimed method. Such a discovery does not render the invention non-obvious. See e.g., MPEP 2145 section II. Thus, the Applicant's arguments in traversal are not found persuasive with reference to the claims generally.

Traversal of the rejection of claim 25

Claim 25 reads on the claimed methods wherein BT is administered at a dose of between 1 and 30 mouse units. The Applicant argues that "it is known that different types of botulinum

toxin are required in different amounts for different applications." The Applicant argues that because of this, it would not be obvious to use the claimed dosages for the claimed methods. This argument is not found persuasive because, as indicated by the Applicant, those in the art are aware of the variability in dosages when using the toxin. Thus, they would be aware that the dosage required for administration to the intrinsic muscles would be different from that administered to larger muscles. See e.g., Aoki et al., columns 8-9 (demonstrating large variability in dosage depending on usage). The Aoki reference further discloses that ranges overlapping with the claimed range are generally administered to smaller muscles. See e.g., id, examples 6, 7, 10-12. Thus, from these teachings, and because those in the art would be aware that such optimization would be necessary, the claimed ranges would be obvious optimization of the claimed method. The rejection is therefore maintained.

11. **(Prior Rejection- Maintained)** Claims 26 and 27 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Donovan, Aoki, Borodic, and Share as applied to claim 9 and 23 above, and further in view of Moyer et al. (WO 00/15245). Claims 26 and 27 further limit the method of the claims described above to embodiments wherein the botulinum toxin is administered, respectively, in a single injection, or as a plurality of injections. The Applicant appears to be traversing the rejection on the grounds that the reference do not teach the administration of the toxin to intrinsic muscles, as was argued above with reference to claims 9, 21, 22, and 24-27. The rejection is therefore maintained for the same reasons as indicated above.

The Applicant further argues that Moyer is irrelevant to the claimed invention as it is discussing "an entirely different type of treatment." The Examiner does not agree with this

description of the teachings. As indicated in the prior action, the reference teaches that the toxin has a wide range of uses. The reference also teaches that a regimen of treatment with BT may include a number of injections. The Applicant appears to assume, that because the reference introduces the paragraph indicating this begins with an assertion that the toxin is useful for treating spastic muscle disorders, the teachings of the paragraph apply only to such treatments. However, the paragraph continues by providing a list of other disorder for which the regimen may be applies. Page 14, lines 21-31. From these teachings, it would be clear to those in the art that BT treatments caused by muscles generally may, if necessary, involve a continuous course of treatment involving multiple administrations. The rejection is therefore maintained.

12. **(Prior Rejection- Maintained)** Claim 28 was rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Donovan, Aoki, Borodic, and Share as applied to claims 9 and 21, and 22 above, and further in view of the teaching of either of De Simone (U.S. Patent 6,037,373), or Ferree (U.S. Application Publication 2002/0032155). Claim 28 describes a method of treating a disc herniation or degenerative disorder by administering to the patient Botulinum toxin, and by also administering to the patient a factor to enhance healing of the disc. The rejection is also expanded to new claim 29, which reads on the method of claim 28, and further identifies what the Applicant asserts are useful growth factors for the treatment of hernias. The Applicant traverses the rejection on the grounds that the references do not teach that the treatment of herniated discs may be improved by preventing the intrinsic spinal muscles from contracting. However, as indicated above and in the prior action, the claims read on methods of treating disorders associated with spinal compression. The art described above teaches that it is

known in the art that back pains, including spinal cord injuries (thus hernias) may be treated or made less painful by the administration of BT to the appropriate muscles. Each of the De Simone and Ferree references teach the treatment of hernias through the administration of growth factors. Thus, it would be obvious to those in the art to treat a person suffering from a disc hernia using both BT and growth hormones.

While the art does not teach that the combination of the two would achieve better results, such improvement would nonetheless follow by following the treatment suggested by the art. Furthermore, the Applicant has not demonstrated that there is any such improvement. The Applicant has demonstrated in the specification on page 10 (example 1) that administration of BT to a hernia patient appeared to help the treatment of the hernia (i.e. hernia healed after administration of the BT). However, there is no evidence that the combination of BT with a growth factor would improve the treatment. Thus, by arguing the enhancement of the treatment by combining the BT treatment with growth factors, the Applicant is arguing a limitation not in the claims, and for which there is no evidentiary support in the application. Further, because it would have been obvious to combine the two treatments in any case, any such benefits would be achieved by the practice of the known methods for treating the disorders. The rejection is therefore maintained, and expanded to new claim 29.

13. **(New Rejection- necessitated by Amendment)** Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Donovan, Aoki, Borodic, and Share as applied to claims 9 and 21, and 22 above, and further in view of the teachings of Yamada et al., U.S. Patent 5,054,486. This newly added claim reads on a method of treating spinal

compression comprising inserting an acupuncture needle between two vertebrae, and then injecting BT into the intrinsic needles. As indicated above, the Donovan, Aoki, Borodic, and Share references render obvious the use of BT in treating back pain caused by spinal compression (including hernias). The Yamada reference teaches the use of a form of acupuncture involving the insertion of an acupuncture needle between vertebrae for the treatment of hernias. Thus, both the use of acupuncture and the use of BT are known in the art for the treatment of back pains, including hernias. In view of this, it would have been prima facie obvious for those in the art to combine the teachings of the references to arrive at the claimed invention.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
January 13, 2004

James C. Housel 1/26/04
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